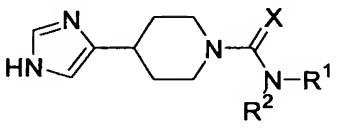
Claims

1. A preventive and/or therapeutic agent for neuropathic pain which comprises, as an active ingredient, a compound having histamine H3-receptor antagonism or a pharmaceutically acceptable salt thereof.

2. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (I):



(I)

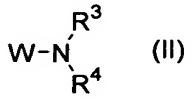
(wherein R^1 and R^2 may be the same or different and each represents a hydrogen atom, substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl, or R^1 and R^2 are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen containing-heterocyclic group;
and X represents an oxygen atom or a sulfur atom).

3. The preventive and/or therapeutic agent for neuropathic pain according to Claim 2, wherein one of R^1 and R^2 is a hydrogen atom, and the other is substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl, and X is a sulfur atom.

4. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having

histamine H3-receptor antagonism is thioperamide.

5. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (II):



(II)

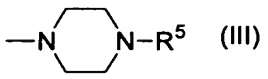
(wherein W represents a residue which imparts antagonistic and/or agonistic activity at histamine H3-receptors when attached to an imidazole ring in 4- or 5-position, and R^3 and R^4 may be the same or different and each represents substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl, or R^3 and R^4 are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen containing-heterocyclic group) or a pharmaceutically acceptable salt thereof.

6. The preventive and/or therapeutic agent for neuropathic pain according to Claim 5, wherein R^3 and R^4 may be the same or different and each is substituted or unsubstituted lower alkyl or substituted or unsubstituted cycloalkyl.

7. The preventive and/or therapeutic agent for neuropathic pain according to Claim 5, wherein R^3 and R^4 are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen-containing

heterocyclic group.

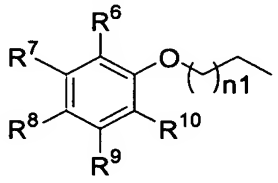
8. The preventive and/or therapeutic agent for neuropathic pain according to Claim 5, wherein $-NR^3R^4$ is a group represented by Formula (III):



(III)

(wherein R^5 represents lower alkyl, cycloalkyl, aryl, aralkyl, lower alkanoyl, cycloalkanoyl, aroyl, lower alkoxycarbonyl or aminoalkylcarbonyl).

9. The preventive and/or therapeutic agent for neuropathic pain according to any of Claims 5 to 8, wherein W is a group represented by Formula (IV):

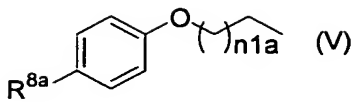


(IV)

(wherein R^6, R^7, R^8, R^9 and R^{10} may be the same or different and each represents a hydrogen atom, halogen, amino, nitro, cyano, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkanoyl, substituted or unsubstituted cycloalkanoyl, substituted or unsubstituted aroyl or substituted or unsubstituted lower alkanoylamino,
and n1 represents an integer of 1 to 7).

10. The preventive and/or therapeutic agent for neuropathic pain according to any of Claims 5 to 8, wherein W is a group

represented by Formula (V):

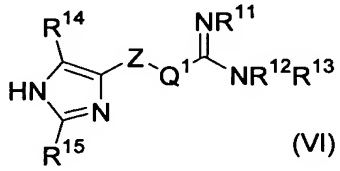


(V)

(wherein R^{8a} has the same meaning as R^8 defined above, and nla has the same meaning as nl defined above).

11. The preventive and/or therapeutic agent for neuropathic pain according to Claim 10, wherein nl is 1 or 2.

12. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (VI):



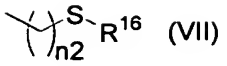
(VI)

[wherein Z represents substituted or unsubstituted lower alkylene;

Q^1 represents a sulfur atom, -NH- or $-CH_2-$;

R^{11}, R^{13} and R^{15} may be the same or different and each represents a hydrogen atom, lower alkyl, cycloalkyl, substituted or unsubstituted aryl or substituted or unsubstituted aralkyl;

R^{12} represents a hydrogen atom, lower alkyl, (cycloalkyl)alkyl, substituted or unsubstituted aryl, substituted or unsubstituted aralkyl or a group represented by Formula (VII):

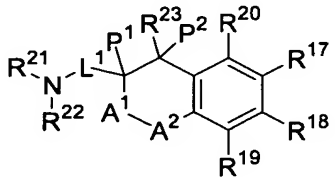


(VII)

(wherein n2 represents an integer of 1 to 4, and R^{16} represents lower alkyl, (cycloalkyl)alkyl or substituted or unsubstituted aralkyl);
and R^{14} represents a hydrogen atom, halogen, amino, nitro, cyano, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted aralkyl] or a pharmaceutically acceptable salt thereof.

13. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is clobenpropit.

14. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (VIII):



(VIII)

{ wherein A^1 represents a bond or carbonyl;
A^2 represents an oxygen atom or a sulfur atom;
L^1 represents lower alkylene which may be substituted by a fluorine atom or hydroxy;
P^1 and P^2 represent hydrogen atoms or are combined to represent a bond;

R^{17}, R^{18}, R^{19} and R^{20} may be the same or different and each represents a hydrogen atom, halogen, nitro, hydroxy, mercapto, cyano, carboxy, lower alkanoyl, lower alkoxycarbonyl, lower alkanoyloxy, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-NR^{24a}R^{24b}$ (wherein R^{24a} and R^{24b} may be the same or different and each represents a hydrogen atom, lower alkyl or lower alkanoyl), $-C(=O)-NR^{24c}R^{24d}$ (wherein R^{24c} and R^{24d} have the same meanings as R^{24a} and R^{24b} defined above, respectively), $-SO_2-NR^{24e}R^{24f}$ (wherein R^{24e} and R^{24f} have the same meanings as R^{24a} and R^{24b} defined above, respectively), $-L^2-R^{25}$ [wherein L^2 represents an oxygen atom, a sulfur atom, lower alkylene, lower alkenylene, $-S(O)-$, $-S(O)_2-$ $-C(O)-$, $-C(=NOR^{26})-$ (wherein R^{26} represents a hydrogen atom or lower alkyl) or $-N(R^{27})-$ (wherein R^{27} represents a hydrogen atom, lower alkyl or lower alkanoyl), and R^{25} represents cycloalkyl, aryl or a heterocyclic group] , or $-L^3-L^4-R^{28}$ [wherein L^3 represents cycloalkylene, arylene, a divalent group formed by removing any one hydrogen atom from an aliphatic heterocyclic group or heteroarylene, L^4 represents a bond, an oxygen atom, a sulfur atom, lower alkylene, lower alkenylene, $-C(O)-$,

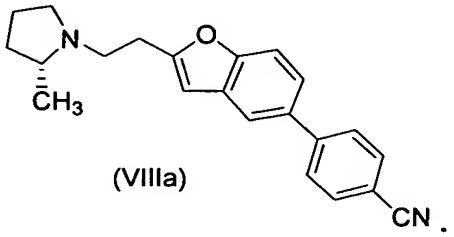
$-C(=NOR^{26a})-$ (wherein R^{26a} has the same meaning as R^{26} defined above) or $-N(R^{27a})-$ (wherein R^{27a} has the same meaning as R^{27} defined above), and R^{28} has the same meaning as R^{25} defined above]; at least one of R^{17}, R^{18}, R^{19} and R^{20} represents cycloalkyl, substituted or unsubstituted aryl, a substituted or unsubstituted heterocyclic group, $-L^2-R^{25}$ (wherein L^2 and R^{25} have the same meanings as defined above, respectively) or $-L^3-L^4-R^{28}$ (wherein L^3, L^4 and R^{28} have the same meanings as defined above, respectively);

R^{21} and R^{22} may be the same or different and each represents a hydrogen atom, lower alkyl, hydroxy-lower alkyl, cycloalkyl, (cycloalkyl)alkyl, lower alkenyl, lower alkynyl, aryl, aralkyl, a heterocyclic group or heterocyclic alkyl, or R^{21} and R^{22} are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen-containing heterocyclic group;

and R^{23} represents a hydrogen atom, halogen, nitro, hydroxy, mercapto, cyano, carboxy, lower alkoxycarbonyl, lower alkanoyl, lower alkanoyloxy, lower alkylsulfinyl, lower alkylsulfonyl, lower alkylthio, aryl, a heterocyclic group, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkoxy, $-NR^{29a}R^{29b}$ (wherein R^{29a} and R^{29b} have the same meanings as R^{24a} and R^{24b} defined above, respectively), $-C(=O)-NR^{29c}R^{29d}$ (wherein R^{29c} and R^{29d} have the same meanings as R^{24a} and R^{24b} defined above, respectively) or

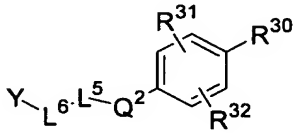
$-SO_2-NR^{29e}R^{29f}$ (wherein R^{29e} and R^{29f} have the same meanings as R^{24a} and R^{24b} defined above, respectively)}.

15. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (VIIIa):



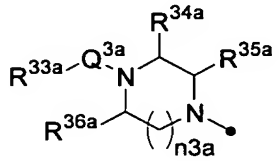
(VIIIa)

16. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (IX):



(IX)

{wherein Y represents a group represented by Formula (X):



(X)

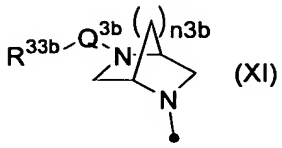
[wherein n3a is 1 or 2;

Q^{3a} represents a bond, -C(O)-, -C(S)-, $-CH_2-$, $-SO_2-$ or $-C(=NR^{37})-$ (wherein R^{37} represents a hydrogen atom, hydroxy, lower alkyl, cycloalkyl, (cycloalkyl)alkyl, lower alkoxy,

aryl or aralkyl);

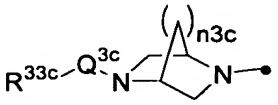
R^{33a} represents a hydrogen atom, amino, lower alkyl, lower alkoxy, cycloalkoxy, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted aryloxy, a substituted or unsubstituted heterocyclic group or $-W^1-C(R^{38a})(R^{38b})-NR^{39a}R^{39b}$ (wherein W^1 represents a bond or substituted or unsubstituted lower alkylene, R^{38a} and R^{38b} may be the same or different and each represents a hydrogen atom, amino, aralkyl or substituted or unsubstituted lower alkyl, and R^{39a} and R^{39b} may be the same or different and each represents a hydrogen atom, aminosulfonyl, lower alkyl, lower alkanoyl, lower alkylsulfonyl, cycloalkyl, (cycloalkyl)alkyl, cycloalkanoyl, cycloalkylsulfonyl, aralkyl, aroyl, arylsulfonyl, heterocyclic alkyl, heterocyclic carbonyl, heterocyclic alkanoyl, heterocyclic sulfonyl, substituted or unsubstituted aryl, a substituted or unsubstituted aromatic heterocyclic group or a substituted or unsubstituted aliphatic heterocyclic group, or R^{39a} and R^{39b} are combined together with the adjacent nitrogen atom thereto to form a substituted or unsubstituted nitrogen-containing heterocyclic group, or R^{38a} or R^{38b} and R^{39a} or R^{39b} are combined together with the adjacent carbon atom and nitrogen atom thereto to form a substituted or unsubstituted heterocyclic group);

and R^{34a}, R^{35a} and R^{36a} may be the same or different and each represents a hydrogen atom or lower alkyl], a group represented by Formula (XI):



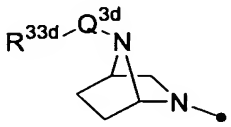
(XI)

(wherein n3b, Q^{3b} and R^{33b} have the same meanings as n3a, Q^{3a} and R^{33a} defined above, respectively), a group represented by Formula (XII):



(XII)

(wherein n3c, Q^{3c} and R^{33c} have the same meanings as n3a, Q^{3a} and R^{33a} defined above, respectively) or a group represented by Formula (XIII):



(XIII)

(wherein Q^{3d} and R^{33d} have the same meanings as Q^{3a} and R^{33a} defined above, respectively);

L^5 represents a bond or lower alkylene which may be substituted by substituted or unsubstituted aryl;

L^6 represents a bond, substituted or unsubstituted lower alkylene, or substituted or unsubstituted cycloalkylene, and L^5 and L^6 do not represent bonds simultaneously;

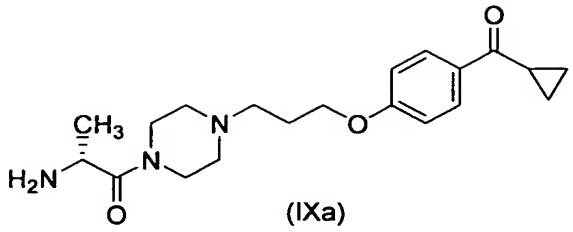
Q^2 represents an oxygen atom, a sulfur atom, $-S(O)-$, $-S(O)_2-$

or -C≡C-;

R^{30} represents halogen, amino, cyano, aminocarbonyl, cycloalkyl, lower alkoxy, lower alkanoyl, cycloalkanoyl, lower alkoxycarbonyl, mono- or di(lower alkyl)aminocarbonyl, aralkyl, aroyl, arylsulfonyl, aromatic heterocyclic carbonyl, aromatic heterocyclic sulfonyl, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl, a substituted or unsubstituted aromatic heterocyclic group, $-CHR^{40a}-OR^{41a}$ (wherein R^{40a} represents a hydrogen atom, lower alkyl, cycloalkyl, (cycloalkyl)alkyl, aryl or aralkyl, and R^{41a} represents a hydrogen atom, lower alkyl, cycloalkyl, (cycloalkyl)alkyl, lower alkanoyl, lower alkoxycarbonyl, tri(lower alkyl)silyl, aryl or aralkyl), or $-C(R^{40b})=N-OR^{41b}$ (wherein R^{40b} and R^{41b} have the same meanings as R^{40a} and R^{41a} defined above, respectively);

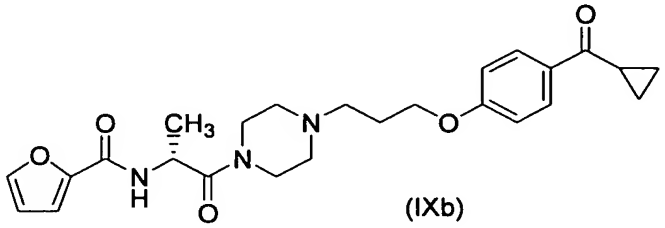
and R^{31} and R^{32} may be the same or different and each represents a hydrogen atom, halogen, amino, nitro, azido, hydroxy, cyano, formyl, carboxy, lower alkyl, perfluoro lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy or perfluoro lower alkoxy, or R^{31} and R^{32} are combined to represent $-OCH_2C(O)-$} .

17. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (IXa):



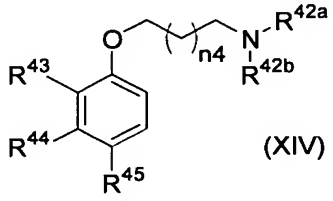
(IXa)

18. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (IXb):



(IXb)

19. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (XIV):



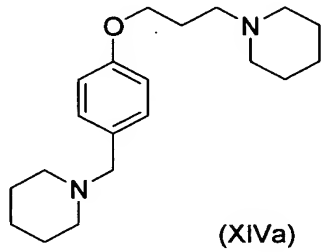
(XIV)

{wherein n4 represents an integer of 0 to 4;
R^{42a} and R^{42b} may be the same or different and each represents lower alkyl, lower alkenyl, cycloalkyl or (cycloalkyl)alkyl, or R^{42a} and R^{42b} are combined together with the adjacent nitrogen atom thereto to form a nitrogen-containing

heterocyclic group;
and two of R^{43}, R^{44} and R^{45} may be the same or different and each represents a hydrogen atom or halogen, and the remainder represents a substituted or unsubstituted heterocyclic group, substituted or unsubstituted heterocyclic alkyl, substituted or unsubstituted heterocyclic alkenyl, substituted or unsubstituted heterocyclic alkynyl, $-L^7-L^8-Q^4$ [wherein L^7 represents a bond or an oxygen atom, L^8 represents substituted or unsubstituted lower alkylene, cycloalkylene, alkenylene or alkynylene, and Q^4 represents an aliphatic heterocyclic group or $-NR^{46a}R^{46b}$ (wherein R^{46a} and R^{46b} may be the same or different and each represents a hydrogen atom, lower alkyl, lower alkenyl, cycloalkyl, (cycloalkyl)alkyl, aryl, aralkyl, a heterocyclic group or heterocyclic alkyl)], $-N(L^{8a}-Q^{4a})R^{47}$ (wherein L^{8a} and Q^{4a} have the same meanings as L^8 and Q^4 defined above, respectively, and R^{47} represents a hydrogen atom, lower alkyl, lower alkenyl, cycloalkyl, (cycloalkyl)alkyl, a heterocyclic group or heterocyclic alkyl) or $-L^9-C(L^{8b}-Q^{4b})R^{48}R^{49}$ (wherein L^{8b} and Q^{4b} have the same meanings as L^8 and Q^4 defined above, respectively, L^9 represents a bond, substituted or unsubstituted lower alkylene, cycloalkylene, alkenylene or alkynylene, R^{48} represents a hydrogen atom, lower alkyl, lower alkenyl, cycloalkyl, (cycloalkyl)alkyl, a heterocyclic group or

heterocyclic alkyl, and R^{49} represents a hydrogen atom, halogen, hydroxy or lower alkoxy)}.

20. The preventive and/or therapeutic agent for neuropathic pain according to Claim 1, wherein the compound having histamine H3-receptor antagonism is a compound represented by Formula (XIVa):



(XIVa)

21. A method for preventing and/or treating neuropathic pain, which comprises administering an effective amount of the compound having histamine H3-receptor antagonism.

22. The method for preventing and/or treating neuropathic pain according to Claim 21, wherein the compound having histamine H3-receptor antagonism is the compound described in any of Claims 2 to 20.

23. Use of a compound having histamine H3-receptor antagonism, for the manufacture of a preventive and/or therapeutic agent for neuropathic pain.

24. The use of a compound having histamine H3-receptor antagonism according to Claim 23, wherein the compound having histamine H3-receptor antagonism is the compound described in any of Claims 2 to 20.